

Applicant : Cawthorne
Serial No. : 09/423,684
Filed : March 20, 2000
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COMPLETE LISTING OF ALL CLAIMS, WITH MARKINGS AND STATUS IDENTIFIERS
(Currently amended claims showing deletions by ~~striketrough~~ and additions by underlining)

1 (original): A method of decreasing body weight in a patient, said method comprising administering a therapeutically effective amount of somatostatin or a somatostatin agonist to said patient.

2 (original): A method of claim 1, wherein said method comprises administering a therapeutically effective amount of a somatostatin agonist to said patient.

3 (original): A method of claim 2, wherein said somatostatin agonist is a somatostatin type-2 receptor agonist.

4 (original): A method of claim 2, wherein said somatostatin agonist is a somatostatin type-5 receptor agonist.

5 (original): A method of claim 3, wherein said somatostatin type-2 receptor agonist has a K_i of less than 2 nM for the somatostatin type-2 receptor.

6 (original): A method of claim 4, wherein said somatostatin type-5 receptor agonist has a K_i of less than 2 nM for the somatostatin type-5 receptor.

7 (original): A method of claim 2, wherein said somatostatin agonist is a somatostatin type-2 receptor selective agonist.

8 (original): A method of claim 2, wherein said somatostatin agonist is a somatostatin type-5 receptor selective agonist.

9 (original): A method of claim 7, wherein said

somatostatin type-2 receptor selective agonist has a K_i for the somatostatin type-2 receptor that is at least 10 times less than the K_i for the somatostatin type-1, type-3, type-4, and type-5 receptors.

10 (original): A method of claim 8, wherein said somatostatin type-5 receptor selective agonist has a K_i for the somatostatin type-5 receptor that is at least 10 times less than the K_i for the somatostatin type-1, type-2, type-3, and type-4 receptors.

11 (original): A method of decreasing body weight in a patient, said method comprising administering a therapeutically effective amount of H-Cys-Phe-Phe-D-Trp-Lys-Thr-Phe-Cys-NH₂, wherein a disulfide bond exists between the free thiols of two Cys residues.

12 (currently amended): A method of claim 1, wherein said patient is ~~an~~ a non-insulin-dependent diabetic human.

13 (currently amended): A method of claim 2, wherein said patient is ~~an~~ a non-insulin-dependent diabetic human.

14 (currently amended): A method of claim 3, wherein said patient is ~~an~~ a non-insulin-dependent diabetic human.

15 (currently amended): A method of claim 4, wherein said patient is ~~an~~ a non-insulin-dependent diabetic human.

16 (currently amended): A method of claim 5, wherein said patient is ~~an~~ a non-insulin-dependent diabetic human.

17 (currently amended): A method of claim 6, wherein said patient is ~~an~~ a non-insulin-dependent diabetic human.

18 (currently amended): A method of claim 7, wherein said patient is ~~an~~ a non-insulin-dependent diabetic human.

19 (currently amended): A method of claim 8, wherein said patient is ~~an~~ a non-insulin-dependent diabetic human.

20 (currently amended): A method of claim 9, wherein said patient is ~~an~~ a non-insulin-dependent diabetic human.

21 (currently amended): A method of claim 10, wherein said patient is ~~an~~ a non-insulin-dependent diabetic human.

22 (currently amended): A method of claim 11, wherein said patient is ~~an~~ a non-insulin-dependent diabetic human.

23 (currently amended): A method according to claim 1 wherein the somatostatin agonist is

H-D- β -Nal-Cys-Tyr-D-Trp-Lys-Thr-Cys-Thr-NH₂,
H-D-Phe-Cys-Phe-D-Trp-Lys-Thr-Cys- β -Nal-NH₂,
H-D-Phe-Cys-Tyr-D-Trp-Lys-Thr-Cys- β -Nal-NH₂,
H-D- β -Nal-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH₂,
H-D-Phe-Cys-Tyr-D-Trp-Lys-Thr-Pen-Thr-NH₂,
H-D-Phe-Cys-Phe-D-Trp-Lys-Thr-Pen-Thr-NH₂,
H-D-Phe-Cys-Tyr-D-Trp-Lys-Thr-Pen-Thr-OH,
H-D-Phe-Cys-Phe-D-Trp-Lys-Thr-Pen-Thr-OH,
H-Gly-Pen-Phe-D-Trp-Lys-Thr-Cys-Thr-OH,
H-Phe-Pen-Tyr-D-Trp-Lys-Thr-Cys-Thr-OH,
H-Phe-Pen-Phe-D-Trp-Lys-Thr-Pen-Thr-OH,
H-D-Phe-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-ol
H-D-Phe-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH₂,
H-D-Trp-Cys-Tyr-D-Trp-Lys-Val-Cys-Thr-NH₂,
H-D-Trp-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH₂,
H-D-Phe-Cys-Tyr-D-Trp-Lys-Val-Cys-Thr-NH₂,
H-D-Phe-Cys-Tyr-D-Trp-Lys-Val-Cys-Trp-NH₂,
H-D-Phe-Cys-Tyr-D-Trp-Lys-Val-Cys-Thr-NH₂,

Ac-D-Phe-Lys⁺-Tyr-D-Trp-Lys-Val-Asp-Thr-NH₂ (an amide bridge formed between Lys⁺ and Asp),

Ac-hArg(Et)₂-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH₂,

Ac-D-hArg(Et)₂-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH₂,

Ac-D-hArg(Bu)-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH₂,

Ac-D-hArg(Et)₂-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH₂,

Ac-L-hArg(Et)₂-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH₂,

Ac-D-hArg(CH₂CF₃)₂-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH₂,

Ac-D-hArg(CH₂CF₃)₂-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH₂,

Ac-D-hArg(CH₂CF₃)₂-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Phe-NH₂,

Ac-D-hArg(CH₂CF₃)₂-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NHET,

Ac-L-hArg(CH₂-CF₃)₂-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH₂,

Ac-D-hArg(CH₂CF₃)₂-Gly-Cys-Phe-D-Trp-Lys(Me)-Thr-Cys-Thr-NH₂,

Ac-D-hArg(CH₂CF₃)₂-Gly-Cys-Phe-D-Trp-Lys(Me)-Thr-Cys-Thr-NHET,

Ac-hArg(CH₃, hexyl)-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH₂,

H-hArg(hexyl)₂-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH₂,

Ac-D-hArg(Et)₂-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NHET,

Ac-D-hArg(Et)₂-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Phe-NH₂,

Propionyl-D-hArg(Et)₂-Gly-Cys-Phe-D-Trp-Lys(iPr)-Thr-Cys-Thr-NH₂,

Ac-D-β-Nal-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Gly-hArg(Et)₂-NH₂,

Ac-D-Lys(iPr)-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH₂,

Ac-D-hArg(CH₂CF₃)₂-D-hArg(CH₂CF₃)₂-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH₂,

Ac-D-hArg(CH₂CF₃)₂-D-hArg(CH₂CF₃)₂-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Phe-NH₂,

Ac-D-hArg(Et)₂-D-hArg(Et)₂-Gly-Cys-Phe-D-Trp-Lys-Thr-Cys-Thr-NH₂,

Ac-Cys-Lys-Asn-4-Cl-Phe-Phe-D-Trp-Lys-Thr-Phe-Thr-Ser-D-Cys-NH₂,

H-Bmp-Tyr-D-Trp-Lys-Val-Cys-Thr-NH₂,

H-Bmp-Tyr-D-Trp-Lys-Val-Cys-Phe-NH₂,

H-Bmp-Tyr-D-Trp-Lys-Val-Cys-p-Cl-Phe-NH₂,

H-Bmp-Tyr-D-Trp-Lys-Val-Cys-β-Nal-NH₂,

H-D-β-Nal-Cys-Tyr-D-Trp-Lys-Val-Cys-Thr-NH₂,

H-D-Phe-Cys-Tyr-D-Trp-Lys-Abu-Cys-Thr-NH₂,

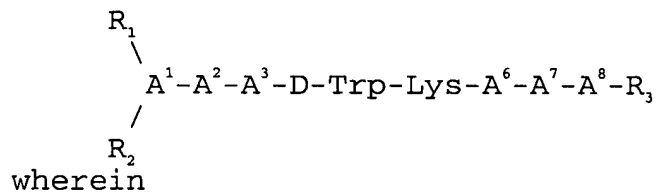
H-D-Phe-Cys-Tyr-D-Trp-Lys-Abu-Cys-β-Nal-NH₂,

H-pentafluoro-D-Phe-Cys-Tyr-D-Trp-Lys-Val-Cys-Thr-NH₂,

Ac-D- β -Nal-Cys-pentafluoro-Phe-D-Trp-Lys-Val-Cys-Thr-NH₂,
 H-D- β -Nal-Cys-Tyr-D-Trp-Lys-Val-Cys- β -Nal-NH₂,
 H-D-Phe-Cys-Tyr-D-Trp-Lys-Val-Cys- β -Nal-NH₂,
 H-D- β -Nal-Cys-Tyr-D-Trp-Lys-Abu-Cys-Thr-NH₂,
 H-D-p-Cl-Phe-Cys-Tyr-D-Trp-Lys-Abu-Cys-Thr-NH₂,
 Ac-D-p-Cl-Phe-Cys-Tyr-D-Trp-Lys-Abu-Cys-Thr-NH₂,
 H-D-Phe-Cys- β -Nal-D-Trp-Lys-Val-Cys-Thr-NH₂,
 H-D-Phe-Cys-Tyr-D-Trp-Lys-Cys-Thr-NH₂,
 cyclo(Pro-Phe-D-Trp-N-Me-Lys-Thr-Phe),
 cyclo(Pro-Phe-D-Trp-N-Me-Lys-Thr-Phe),
 cyclo(Pro-Phe-D-Trp-Lys-Thr-N-Me-Phe),
 cyclo(N-Me-Ala-Tyr-D-Trp-Lys-Thr-Phe),
 cyclo(Pro-Tyr-D-Trp-Lys-Thr-Phe),
 cyclo(Pro-Phe-D-Trp-Lys-Thr-Phe),
 cyclo(Pro-Phe-L-Trp-Lys-Thr-Phe) (SEQ ID NO:1),
 cyclo(Pro-Phe-D-Trp(F)-Lys-Thr-Phe),
 cyclo(Pro-Phe-Trp(F)-Lys-Thr-Phe) (SEQ ID NO:2),
 cyclo(Pro-Phe-D-Trp-Lys-Ser-Phe),
 cyclo(Pro-Phe-D-Trp-Lys-Thr-p-Cl-Phe),
 cyclo(D-Ala-N-Me-D-Phe-D-Thr-D-Lys-Trp-D-Phe),
 cyclo(D-Ala-N-Me-D-Phe-D-Val-Lys-D-Trp-D-Phe),
 cyclo(D-Ala-N-Me-D-Phe-D-Thr-Lys-D-Trp-D-Phe),
 cyclo(D-Abu-N-Me-D-Phe-D-Val-Lys-D-Trp-D-Tyr),
 cyclo(Pro-Tyr-D-Trp-t-4-AchxAla-Thr-Phe),
 cyclo(Pro-Phe-D-Trp-t-4-AchxAla-Thr-Phe),
 cyclo(N-Me-Ala-Tyr-D-Trp-Lys-Val-Phe),
 cyclo(N-Me-Ala-Tyr-D-Trp-t-4-AchxAla-Thr-Phe),
 cyclo(Pro-Tyr-D-Trp-4-Amphe-Thr-Phe),
 cyclo(Pro-Phe-D-Trp-4-Amphe-Thr-Phe),
 cyclo(N-Me-Ala-Tyr-D-Trp-4-Amphe-Thr-Phe),
 cyclo(Asn-Phe-Phe-D-Trp-Lys-Thr-Phe-Gaba),
 cyclo(Asn-Phe-Phe-D-Trp-Lys-Thr-Phe-Gaba-Gaba),
 cyclo(Asn-Phe-D-Trp-Lys-Thr-Phe),
 cyclo(Asn-Phe-Phe-D-Trp-Lys-Thr-Phe-NH(CH₂)₄CO),
 cyclo(Asn-Phe-Phe-D-Trp-Lys-Thr-Phe- β -Ala),

cyclo(Asn-Phe-Phe-D-Trp-Lys-Thr-Phe-D-Glu)-OH,
 cyclo(Phe-Phe-D-Trp-Lys-Thr-Phe),
 cyclo(Phe-Phe-D-Trp-Lys-Thr-Phe-Gly),
 cyclo(Phe-Phe-D-Trp-Lys-Thr-Phe-Gaba),
 cyclo(Asn-Phe-Phe-D-Trp-Lys-Thr-Phe-Gly),
 cyclo(Asn-Phe-Phe-D-Trp(F)-Lys-Thr-Phe-Gaba),
 cyclo(Asn-Phe-Phe-D-Trp(NO₂)-Lys-Thr-Phe-Gaba),
 cyclo(Asn-Phe-Phe-Trp(Br)-Lys-Thr-Phe-Gaba) (SEQ ID NO:3),
 cyclo(Asn-Phe-Phe-D-Trp-Lys-Thr-Phe(I)-Gaba),
 cyclo(Asn-Phe-Phe-D-Trp-Lys-Thr-Tyr(But)-Gaba),
 cyclo(Bmp-Lys-Asn-Phe-Phe-D-Trp-Lys-Thr-Phe-Thr-Pro-Cys)-OH,
 cyclo(Bmp-Lys-Asn-Phe-Phe-D-Trp-Lys-Thr-Phe-Thr-Pro-Cys)-OH,
 cyclo(Bmp-Lys-Asn-Phe-Phe-D-Trp-Lys-Thr-Phe-Thr-Tpo-Cys)-OH,
 cyclo(Bmp-Lys-Asn-Phe-Phe-D-Trp-Lys-Thr-Phe-Thr-MeLeu-Cys)-OH,
 cyclo(Phe-Phe-D-Trp-Lys-Thr-Phe-Phe-Gaba),
 cyclo(Phe-Phe-D-Trp-Lys-Thr-Phe-D-Phe-Gaba),
 cyclo(Phe-Phe-D-Trp(5F)-Lys-Thr-Phe-Phe-Gaba),
 cyclo(Asn-Phe-Phe-D-Trp-Lys(Ac)-Thr-Phe-NH-(CH₂)₃-CO),
 cyclo(Lys-Phe-Phe-D-Trp-Lys-Thr-Phe-Gaba),
 cyclo(Lys-Phe-Phe-D-Trp-Lys-Thr-Phe-Gaba),
 cyclo(Orn-Phe-Phe-D-Trp-Lys-Thr-Phe-Gaba),
 H-Cys-Phe-Phe-D-Trp-Lys-Thr-Phe-Cys-NH₂,
 H-Cys-Phe-Phe-D-Trp-Lys-Ser-Phe-Cys-NH₂,
 H-Cys-Phe-Tyr-D-Trp-Lys-Thr-Phe-Cys-NH₂ or
 H-Cys-Phe-Tyr(I)-D-Trp-Lys-Thr-Phe-Cys-NH₂.

24 (original): A method according to claim 1
 wherein the somatostatin agonist is



A¹ is a D- or L- isomer of Ala, Leu, Ile, Val, Nle, Thr,
 Ser, β-Nal, β-Pal, Trp, Phe, 2,4-dichloro-Phe, pentafluoro-Phe,

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p-X-Phe, or o-X-Phe, wherein X is CH₃, Cl, Br, F, OH, OCH₃ or NO₂;
 A² is Ala, Leu, Ile, Val, Nle, Phe, β-Nal, pyridyl-Ala, Trp,
 2,4-dichloro-Phe, pentafluoro-Phe, o-X-Phe, or p-X-Phe, wherein X
 is CH₃, Cl, Br, F, OH, OCH₃ or NO₂;

A³ is pyridyl-Ala, Trp, Phe, β-Nal, 2,4-dichloro-Phe,
 pentafluoro-Phe, o-X-Phe, or p-X-Phe, wherein X is CH₃, Cl, Br,
 F, OH, OCH₃ or NO₂;

A⁶ is Val, Ala, Leu, Ile, Nle, Thr, Abu, or Ser;

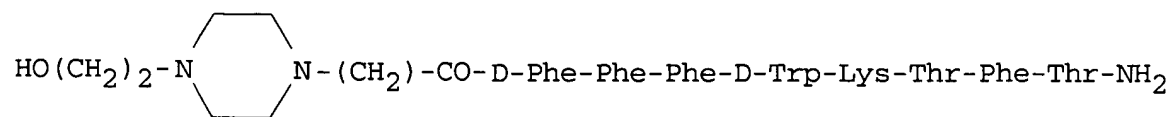
A⁷ is Ala, Leu, Ile, Val, Nle, Phe, β-Nal, pyridyl-Ala, Trp,
 2,4-dichloro-Phe, pentafluoro-Phe, o-X-Phe, or p-X-Phe, wherein X
 is CH₃, Cl, Br, F, OH, OCH₃ or NO₂;

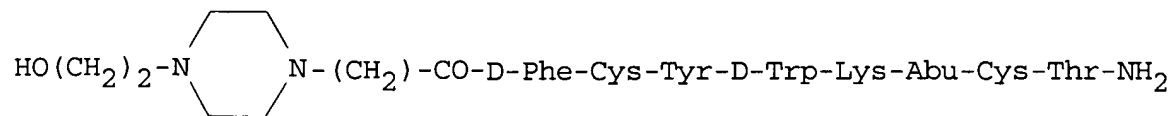
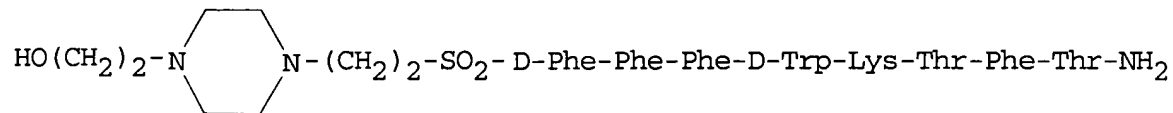
A⁸ is a D- or L-isomer of Ala, Leu, Ile, Val, Nle, Thr, Ser,
 Phe, β-Nal, pyridyl-Ala, Trp, 2,4-dichloro-Phe, pentafluoro-Phe,
 p-X-Phe, or o-X-Phe, wherein X is CH₃, Cl, Br, F, OH, OCH₃ or NO₂;

each R₁ and R₂, independently, is H, lower acyl or lower
 alkyl; and R₃ is OH or NH₂; provided that at least one of A¹ and A⁸
 and one of A² and A⁷ must be an aromatic amino acid; and further
 provided that A¹, A², A⁷ and A⁸ cannot all be aromatic amino acids.

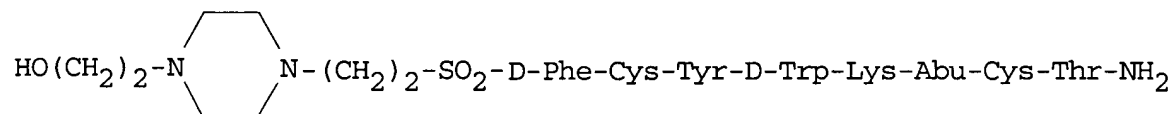
25 (original): A method according to claim 24
 wherein the linear somatostatin agonist is
 H-D-Phe-p-chloro-Phe-Tyr-D-Trp-Lys-Thr-Phe-Thr-NH₂,
 H-D-Phe-p-NO₂-Phe-Tyr-D-Trp-Lys-Val-Phe-Thr-NH₂,
 H-D-Nal-p-chloro-Phe-Tyr-D-Trp-Lys-Val-Phe-Thr-NH₂,
 H-D-Phe-Phe-Phe-D-Trp-Lys-Thr-Phe-Thr-NH₂,
 H-D-Phe-Phe-Tyr-D-Trp-Lys-Val-Phe-Thr-NH₂,
 H-D-Phe-p-chloro-Phe-Tyr-D-Trp-Lys-Val-Phe-Thr-NH₂ or
 H-D-Phe-Ala-Tyr-D-Trp-Lys-Val-Ala-β-D-Nal-NH₂.

26 (original): A method according to claim 1
 wherein the somatostatin agonist is





or



27 (original): A method according to claim 1 wherein said patient is obese.

28 (original): A method according to claim 3 wherein said patient is obese.

29 (original): A method according to claim 4 wherein said patient is obese.

30 (original): A method according to claim 7 wherein said patient is obese.

31 (original): A method according to claim 8 wherein said patient is obese.

32 (original): A method according to claim 11 wherein said patient is obese.

33 - 37 (canceled)